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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/436,892	11/09/1999	RUSSELL M. MEDFORD	04676.105045	7272

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EXAMINER	
GABEL, GAILENE	
ART UNIT	**PAPER NUMBER**
1641	16

DATE MAILED: 11/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/436,892	MEDFORD ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *7,8,11-14 and 16-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9,10,15 and 21-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-36* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 15 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/9/02 has been entered.

Amendment Entry

2. Applicant's amendment and response filed 8/9/02 in Paper No. 14 is acknowledged and has been entered. Claims 1, 4-6, 9, 15, 21-24, 25, 26, and 29-36 have been amended. Claims 1-36 are pending. Claims 7-8, 11-14, 16-20 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Claims 1-6, 9-10, 15, and 21-36 are under examination.

Rejections Withdrawn

Claim Rejections - 35 USC § 102

3. In light of Applicant's amendment and arguments, the rejection of claims 1-3, 6, 21-22, 23-24 and 28 under 35 U.S.C. 102(b) as being inherently anticipated by MAO et al. (WO 95/15760) is hereby withdrawn.

4. In light of Applicant's amendment and arguments, the rejection of claims 1-3, 6, 21-22, 23-24 and 28 under 35 U.S.C. 102(b) as being inherently anticipated by OATES et al. (The New England Journal of Medicine, 1988) is hereby withdrawn.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-6, 9-10, 15, and 21-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Independent claim 1 with dependent claims 2-5 and 21-22:

Claim 1, preamble lacks antecedent support in reciting, "the low density lipoprotein receptor".

Regarding claim 1, the phrase "or other animal" renders the claim indefinite because the claim includes elements not actually disclosed (those encompassed by "or other"), thereby rendering the scope of the claim unascertainable. See MPEP § 2173.05(d).

Claim 1, step c) lacks clear antecedent support in reciting, "the binding of the compound to the CC-LDL (cholesterol-containing low -density lipoprotein)".

Claim 1, step c) is vague and indefinite in reciting, "determining whether the binding of the compound to the CC-LDL forms a complex" because it implies but fails to distinctly and positively define that the compound binds CC-LDL, so as to obtain and isolate CC-LDL from the host. Perhaps, Applicant intends, "determining whether binding has occurred between the compound and the CC-LDL from the host; thus, forming a complex".

Claim 1 step d) is confusing in relation to the preamble because step d) recites that "the binding ... which results in a change in the three dimensional conformation of the lipoprotein ...enhances the binding affinity of the lipoprotein to the "the low density lipoprotein (LDL) receptor" whereas in the preamble, the binding (which causes a change in the three dimensional conformation of the lipoprotein) "enhances clearing of the CC-LDL". Please clarify.

Claim 2 is indefinite in lacking clear antecedent support in reciting, "the LDL". Perhaps, Applicant intends "the CC-LDL" for consistency in claim language.

Claim 3 is indefinite in lacking clear antecedent support in reciting, "the cholesterol-containing lipoprotein". Perhaps, Applicant intends "the CC-LDL" for consistency in claim language.

Claim 22 lacks clear antecedent support in reciting, "the lipoprotein receptor". Perhaps, Applicant intends "the LDL receptor" for consistency in claim language.

B) Independent claim 6 with dependent claims 10, 23-28 and 30;

Claim 6, step iii) is indefinite in lacking clear antecedent support in reciting, "the lipoprotein". Perhaps, Applicant intends "the LDL" for consistency in claim language.

Claim 6, step iii) has improper antecedent basis problem in reciting, "a lipoprotein receptor". Perhaps, Applicant intends "the LDL receptor" for consistency and proper antecedent basis in claim language.

Claim 6 step iii) is confusing in relation to the preamble because step iii) recites that "the (binding) complex ... which alters the three dimensional conformation of the lipoprotein ...enhances the binding of the lipoprotein to the LDL receptor" whereas in the preamble, the binding (which causes a change in the three dimensional conformation of the lipoprotein) "increases the clearance of the LDL". Please clarify.

Claim 23 lacks antecedent support in reciting, "the lipoprotein". Perhaps, Applicant intends "the LDL" for consistency in claim language.

Claim 24 lacks antecedent support in reciting, "the lipoprotein receptor". Perhaps, Applicant intends "the LDL receptor" for consistency in claim language.

Claim 28 lacks antecedent support in reciting, "the lipoprotein receptor".

Claim 30 lacks clear antecedent support in reciting, "the CC-LDL". Specifically, there is no requirement in this set of claims that the LDL is "cholesterol containing LDL".

C) Independent claim 9 with dependent claims 29 and 33-34;

Claim 9 is indefinite and confusing because it fails to distinctly and clearly define the structural and functional relationship between "a CC-LDL" in the preamble and

"LDL" in step i). If the two elements are meant to encompass the same element, consistency in claim language is suggested for definiteness. See also steps ii), v), and vi) for the term "LDL".

Claim 9 is ambiguous and incomplete for omitting essential structural and functional cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. Specifically, it is unclear, in the claimed sandwich assay, how detection is effected in the absence of a label.

Claim 9, steps ii) - v) is confusing in reciting, "carrying out a sandwich immunoreactivity assay" because the recitation that the "second capture antibody ... binds to the first antibody", does not appear to embody a "sandwich assay". Please clarify. It is further unclear how detection in step iv) is effected using the "second capture antibody" and how the "complex" comprising the first antibody, the CC-LDL, and the compound is formed so as to embody a sandwich (assay) for capture of the second antibody.

Claim 9 is incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. A correlation step which correlates the requirement of the preamble is missing since it is unclear how "comparing the amount of LDL captured by the assay to a control" determines that a change in the structure of apolipoprotein B-100 in a CC-LDL has occurred.

Claim 33 lacks clear antecedent support in reciting, "the apolipoprotein" since there does not appear to be a prior recitation of an "apolipoprotein". Perhaps Applicant

intends that "the CC-LDL (claim 9 preamble) is apoB-100". Refer also to comments and problems in claim 9 from which claim 33 depends.

Claim 34 lacks clear antecedent support in reciting, "the lipoprotein receptor" since there does not appear to be a prior recitation of a "lipoprotein receptor". Claim 9 from which claim 34 depends recites "LDL receptor".

D) Independent claim 15 with dependent claims 31-32 and 35-36.

Claim 15 is indefinite and confusing because it fails to distinctly and clearly define the structural and functional relationship between "the lipoprotein" in the preamble and "a cholesterol-containing lipoprotein" in step a). If the two elements are meant to encompass the same element, consistency in claim language is suggested for definiteness. See also step c) in the second occurrence of the term "the lipoprotein".

Claim 35 lacks clear antecedent support in reciting, "the CC-LDL" since there is no previous recitation of "CC-LDL" in this given set of claims.

Claim 36 lacks clear antecedent support in reciting, "the CC-LDL" since there is no previous recitation of "CC-LDL" in this given set of claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The claims are drawn to a method wherein a compound is administered to a human host to enhance clearing of cholesterol-containing low density lipoproteins, from here on CC-LDL. The CC-LDL is isolated from the host and is determined for a change in the three dimensional conformation of the lipoprotein, wherein a change in the three dimensional conformation of the lipoprotein is detected by antibody binding to a specific epitope of the lipoprotein, i.e. apoB-100, which subsequently binds the LDL receptor. The claimed invention purports this mechanism to enhancing the clearance of LDL. At page 14 of the specification, the compounds are identified as monosuccinic acid esters of probucol. Accordingly,

6. Claims 1-6, 9-10, 15, and 21-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parthasarathy (US 5,262,439) in view of Koren et al. (US 6,107,045).

Parthasarathy discloses compounds comprising water-soluble probucol derivatives that are administered for use as LDL clearance drugs. These LDL clearance

drugs are monosuccinic acid esters of probucol which are generally preferred for their ease in synthesis and increased solubility (see Abstract, column 5, lines 24-45, and column 9, lines 9-42). Further, the lipid soluble probucol compounds are preferred to readily hydrolyze in physiological environments so as to be taken up by lipoproteins and lipid containing substances (see column 4, lines 4-11 and column 5, lines 24-48).

Parthasarathy differs from the instant invention in failing to disclose isolating LDL and determining the amount of LDL after administration in vivo, or addition in vitro, of the probucol compound.

Koren et al. disclose quantifying immunoreactive concentrations of lipoprotein and apolipoprotein, including apoB-100 (LDL and VLDL) using sandwich immunoreactivity assays wherein antibodies specific to apoB-100 (known to be important in LDL receptor binding process) are immobilized into microwells as capture antibodies and labeled as secondary antibodies to capture and quantify the LDL concentration, respectively (see columns 11-12). Immunoreactive concentration of LDL is determined by ELISA or polyacrylamide gel electrophoresis (see columns 13, 18, and 20).

One of ordinary skill in the art at the time of the instant invention would have been motivated to use the sandwich immunoassay or agarose electrophoresis methods disclosed by Koren to detect binding of the probucol compounds taught by Parthasarathy to LDL because Koren specifically disclosed that his assay provides antibodies specific for epitopes required for quantitation of LDL, VLDL, or apoB-100 for use in determining accurate antigenic levels in serum and plasma samples.

Additionally, "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old known composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art". Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999). Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure of the compound, i.e. monosuccinic esters of probucol, the properties Applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

While the prior disclosure was silent as to the binding of the compound to LDL which enhances LDL clearance after subsequent binding to the LDL receptor; the instant claims merely recite a newly discovered mechanism --- which results to enhanced clearing of LDL -- a known composition and method for the same use. The claimed process is not directed to a new use, it is the same use and it consists of the same method as described by Parthasarathy. Specifically, newly discovered results of known processes directed to the same purpose are not patentable because such results are inherent. The claim language is only a statement of purpose and intended result. The expression does not result in a manipulative difference in the steps of the claims.

Response to Arguments

7. Applicant's arguments have been considered but are moot in view of the new grounds of rejection.

8. For reasons aforementioned, no claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday-Thursday from 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
November 19, 2002
Art Unit 1641

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641